DEPARTMENT OF HEALTH AND HUMAN SERVICES

Reference Number: 95-0458

OCT 2 1996

Barry D. Garfinkle, Ph.D.
Merck & Co., Inc.
Sumneytown Pike
West Point, PA 19486

Dear Dr. Garfinkle:

Enclosed is a product license authorizing Merck & Co., Inc., U.S. License No. 2, to manufacture and ship Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine for sale, barter, or exchange in interstate and foreign commerce.

Under this license you are authorized to manufacture Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine, trade name COMVAX™, for the immunization of persons 6 weeks to 15 months of age born to hepatitis B surface antigen (HBsAg) negative mothers. The product will be marketed in 0.5 ml single dose vials, containing 7.5 mcg Haemophilus b polysaccharide and 5 mcg HBsAg per dose.

You are requested to submit final container samples of the product and samples of the Haemophilus b Conjugate monovalent bulk and the Hepatitis B (Recombinant) monovalent bulk along with protocols showing results of all applicable tests. No lots of product shall be distributed until notification of release is received from the Director, Center for Biologics Evaluation and Research (CBER).

The dating period for this product shall be 18 months from the date of manufacture when stored at 2-8°C. The date of manufacture is defined as the date of final container filling from monovalent components which have met specifications for potency. Prior to final container filling, the monovalent bulks may be stored for 12 months at 2-8°C. We understand that your release protocols will be modified to include the date of manufacture for final container and each bulk intermediate, and that extension of these dating and storage periods will be based upon the submission of additional data to be discussed with CBER.

Changes in the manufacture, testing, packaging, or labeling of COMVAX™ or in the manufacturing facilities may require the submission of a Supplement to either your Product or Establishment License Application for our review and written approval prior to implementation.

We acknowledge the following commitments made in your correspondence of September 19, 24, and 26, 1996:

1. You have agreed to submit within 6 months a protocol to IND 3576 for a Phase 4 study to obtain safety data in an additional 5,000 infants 2 to 15 months of age, who will receive three doses of COMVAX™.

2. You have agreed to investigate a modification of the lot release testing for the Haemophilus b component in the final container. Until that modification is in place, the polysaccharide content of the aluminum hydroxide-adsorbed 45 mcg/ml bulk will be measured by a chemical assay. The identity test on the product in final container will be its reaction with specific antiserum detected by EIA. The specification for polysaccharide antigen content will be 10.5 to 19.5 mcg/ml. The process of dilution from the 45 mcg/ml bulk to the 15 mcg/ml final container will be confirmed by analysis of the protein concentration of both the bulk and the final container.

3. You have agreed to submit for review by CBER the results of on-going studies to evaluate immunogenicity of Varicella Vaccine, Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine (primary immunization), and Polio Virus Vaccine Inactivated when administered concurrently with COMVAX™. You have agreed to submit the summary reports of these studies by December 31, 1996, to IND 3576. You have also agreed to revise the package insert for COMVAX™ to include the results of these studies on concurrent immunization of COMVAX™ with these pediatric vaccines.

This information will be placed on file in your Product License Application for this product.

It is requested that adverse experience reports for Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). Since your product is categorized as a vaccine, these reports should be submitted to the Vaccine Adverse Event Reporting System (VAERS) using the pre-addressed form VAERS-1.

Please submit three copies of final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition, please submit three copies of the introductory advertising and promotional labeling. You may wish to submit the proposed materials in draft form with an FDA form 2567 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Promotional claims should be consistent with and not contrary to approved labeling. No comparative claims or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Please acknowledge receipt of the enclosed product license to the Director, Division of Vaccines and Related Products Applications, HFM-475, Center for Biologics Evaluation and Research.

Sincerely yours,

M. Carolyn Hardegree, M.D.
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research